

Positive Results Announced in Largest Pivotal Phase 3 Trial of a First-in-Class Oral Antibiotic to Treat Uncomplicated Gonorrhoea

- A phase 3 study of oral zoliflodacin met the primary endpoint when compared against the combination of injectable ceftriaxone and oral azithromycin, a current international standard of care.
- Positive top-line study results are a significant milestone in the development of a first-in-class antibiotic against drug-resistant *Neisseria gonorrhoeae*, a high priority pathogen.
- Groundbreaking antibiotic research and development partnership model paves the way for development of other antibiotics to address impact of antimicrobial resistance (AMR).

Geneva (Switzerland) and Waltham, MA (USA), 1 November 2023 – The Global Antibiotic Research & Development Partnership (GARDP) in collaboration with Innoviva Specialty Therapeutics, a subsidiary of Innoviva, Inc. (Nasdaq: INVA), announced today that zoliflodacin, a first-in-class antibiotic, met its primary endpoint in an unprecedented global pivotal phase 3 clinical trial. Study investigators found that oral zoliflodacin demonstrated statistical non-inferiority of microbiological cure at the urogenital site when compared to treatment with intramuscular (IM) injection of ceftriaxone and oral azithromycin, a current global standard of care regimen. In the study, zoliflodacin was found to be generally well tolerated and there were no serious adverse events or deaths recorded in the trial.

This is the first study to address a World Health Organization priority pathogen that has been sponsored and led by a non-profit organization. These positive preliminary findings offer hope for patients with this condition, particularly in the face of rising antibiotic resistance to current regimens. It also paves the way for a new research and development model in the global fight against antimicrobial resistance (AMR). If approved, zoliflodacin will be the first new antibiotic for treating gonorrhoea in decades.

“This is a significant step forward in the treatment of gonorrhoea, and also shows that GARDP’s public-private partnership model can play a crucial role in helping to fix the public health failure at the heart of the global AMR crisis,” said Dr. Manica Balasegaram, Executive Director of GARDP. “Despite the extremely high public health value, there has been a lack of investment to develop new drugs for gonorrhoea. This zoliflodacin programme demonstrates that it is possible to develop antibiotic treatments targeting multidrug-resistant bacteria that pose the greatest public health threat, and which may not otherwise get developed.”

With more than 82 million new gonorrhoea infections occurring globally each year, gonorrhoea is the third most common sexually transmitted infection, affecting both men and women in ways that can result in serious and permanent health consequences. The bacterium *Neisseria gonorrhoeae* has gradually developed resistance to many classes of antibiotics used to treat these infections and as a result, ceftriaxone, given as a single intramuscular injection, has become the last available recommended treatment for gonorrhoea globally.

“The outcome of this study is a potential game changer for sexual health,” said Edward W. Hook III, MD, Protocol Chair for the study and Emeritus Professor of Medicine at the University of Alabama, in Birmingham. “In addition to the potential benefits for patients with infections with resistant strains of *Neisseria gonorrhoeae*, the potential lack of cross-resistance with other antibiotics and the oral route of administration will simplify gonorrhoea therapy for clinicians worldwide.”

Recent reports ([The Lancet Infectious Diseases](#)) of emergent ceftriaxone-resistant infections have heightened the urgency for new antibiotics. Effective treatment options are essential to reducing the burden of disease for individuals, and to preventing the spread of highly drug-resistant gonorrhoea globally. If left untreated, gonorrhoea can also cause infertility in women, life-threatening ectopic pregnancies, and pelvic inflammatory disease.

“The success of this study could have a profound effect on how physicians approach gonorrhoea infections, as an oral alternative to an injection could improve patient access and compliance, as well as help reduce the increasing spread of antibiotic resistant strains of the disease,” said Pavel Raifeld, Chief Executive Officer, Innoviva, Inc. “Such a positive outcome represents an important milestone for Innoviva Specialty Therapeutics and reinforces our position as a premier infectious disease and critical care company.”

Zoliflodacin has a unique mechanism of action in the way that it inhibits a crucial bacterial enzyme called type II topoisomerase, which is essential for bacterial function and reproduction. Previous in-vitro studies have shown that it is active against multidrug-resistant strains of *Neisseria gonorrhoeae*, including those resistant to ceftriaxone, and azithromycin, with no cross-resistance with other antibiotics. Now, the positive results of this landmark phase 3 trial confirm that zoliflodacin has the potential to tackle the most difficult-to-treat gonorrhoea infections.

The phase 3 trial enrolled a total of 930 patients with uncomplicated gonorrhoea, including women, adolescents and people living with HIV, making it the largest clinical trial ever conducted for a new treatment against gonorrhoea infection, with 16 trial sites in regions with a high prevalence of gonorrhoea across five countries, including Belgium, the Netherlands, South Africa, Thailand, and the U.S. The trial compared a single oral suspension 3g dose of zoliflodacin to a globally recognized standard of care regimen (500mg ceftriaxone IM plus 1g oral azithromycin) for the treatment of uncomplicated gonorrhoea.

Zoliflodacin met the prespecified statistical test for non-inferiority when compared to ceftriaxone and oral azithromycin (5.31% (95%CI 1.38, 8.65%)). Non-inferiority of zoliflodacin was demonstrated within the pre-specified margin of 12% and, furthermore, within the margin of 10% as specified in U.S. Food and Drug Administration guidance.

GARDP has the right to register and commercialize the product in more than three-quarters of the world's countries, including all low-income countries, most middle-income countries, and several high-income countries. GARDP is committed to work with its partners and local health authorities in markets where zoliflodacin receives regulatory approval, to help remove access barriers to ensure treatment is available to address unmet medical needs while ensuring appropriate and sustainable use. Entasis Therapeutics Limited, an affiliate of Innoviva Specialty Therapeutics, retains the commercial rights for zoliflodacin in the major markets in North America, Europe, Asia-Pacific, and Latin America.



This GARDP-led trial was funded with support from the governments of Germany (BMBF and BMG), UK (GAMRIF, part of DHSC, and DFID), Japan (MHLW), the Netherlands (Ministries of VWS and BZ), Switzerland (FOPH), The Grand Duchy of Luxembourg, as well as the Canton of Geneva, South African Medical Research Council (SAMRC), and the Leo Model Foundation. This builds on the critical phase 2 clinical trial sponsored by the U.S. National Institute of Allergy and Infectious Diseases (NIAID).

About GARDP

The Global Antibiotic Research & Development Partnership (GARDP) is a Swiss not-for-profit organization developing new treatments for drug-resistant infections that pose the greatest threat to health. GARDP was created by the World Health Organization and the Drugs for Neglected Diseases initiative (DNDi) in 2016 and legally founded in 2018 to ensure that everyone who needs antibiotics receives effective and affordable treatment. GARDP is funded by the governments of Australia, Germany, Japan, Monaco, the Netherlands, the Public Health Agency of Canada, South Africa, Switzerland, the United Kingdom, the Canton of Geneva, as well as the European Union, Wellcome Trust and private foundations. GARDP is registered under the legal name GARDP Foundation. <http://www.gardp.org/>

About Innoviva Specialty Therapeutics

Innoviva Specialty Therapeutics, a subsidiary of Innoviva, Inc., is focused on delivering innovative therapies in critical care and infectious disease. Innoviva Specialty Therapeutics' products, through its affiliate, La Jolla Pharmaceutical Company, include GIAPREZA® (angiotensin II), approved to increase blood pressure in adults with septic or other distributive shock, and XERAVA® (eravacycline) for the treatment of complicated intra-abdominal infections in adults. Innoviva Specialty Therapeutics' products, through its affiliate, Entasis Therapeutics Inc., include XACDURO® (sulbactam for injection; durlobactam for injection), co-packaged for intravenous use approved for the treatment of adults with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia caused by susceptible strains of *Acinetobacter baumannii-calcoaceticus* complex (*Acinetobacter*). Our Phase 3 development pipeline includes, zoliflodacin, a novel treatment for uncomplicated gonorrhoea in adults. For more information about Innoviva Specialty Therapeutics, please visit [here](#).

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